(19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 13 October 2005 (13.10.2005)

PCT

(10) International Publication Number WO 2005/095344 A1

- (51) International Patent Classification⁷: C07D 213/73, 405/12, 411/12, A61K 31/44, 31/443, A61P 35/00
- (21) International Application Number:

PCT/US2005/009966

- (22) International Filing Date: 23 March 2005 (23.03.2005)
- (25) Filing Language:
- (26) Publication Language:

English

English

(30) Priority Data:

60/556,218

24 March 2004 (24.03.2004) US

- (71) Applicant (for all designated States except US): ARRAY BIOPHARMA INC. [US/US]; 3200 Walnut Street, Boulder, CO 80301 (US).
- (72) Inventor; and
- (75) Inventor/Applicant (for US only): BOYD, Steven A. [US/US]; 5665 St. Vrain Road, Longmont, CO 80503 (US)
- (74) Agent: HALEY, James F., Jr.; Fish & Neave IP Group, Ropes & Gray LLP, 1251 Avenue of the Americas, New York, NY 10020 (US).

- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: THIOALKENEAMIDES AS TRANSKETOLASE INHIBITORS

$$\begin{array}{c|c}
R^{1} & R^{2} & O \\
 & & & & \\
R^{4} & & & & \\
R^{b} & & & & \\
R^{b} & & & & \\
R^{c} & &$$

(57) Abstract: The present invention provides thioalkeneamides of formula (I) which are useful as transketolase inhibitors: wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^a - R^d , n and ring A are as defined herein. The present invention also provides pharmaceutical compositions comprising the compounds of formula (I). The invention provides methods for inhibiting transketolase activity, reducing cellular ribose-5-phosphate levels, inhibiting nucleic acid synthesis, inhibiting cell proliferation and tumor cell growth in vitro and in vivo, stimulating apoptosis in tumor cells and treating cancer by administering a compound of formula (I) or a pharmaceutical composition thereof.

